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Use of Data from Predictive Tests following Fetoscopic Endoluminal Tracheal Occlusion for Congenital Diaphragmatic Hernia

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We have read with interest the recent papers by our partners in the European Program on Soft Tissue Engineering for Children (EuroSTEC – www.eurostec.eu) on the prognostic value of pulmonary Doppler in predicting survival and morbidity of fetoscopic endoluminal tracheal occlusion (FETO) in fetuses with severe isolated left congenital diaphragmatic hernia (CDH) and liver herniation. The value of pulmonary circulation assessment for the prediction of outcome of fetal therapy has been investigated either by using Doppler to evaluate blood vessel resistance and/or actual blood flow, or as response to maternal hyperoxygenation [1–3].

On a theoretical basis, the investigation of pulmonary circulation provides independent information that can be combined with that already obtained by measuring the size of the airway compartment and/or the position of the liver. Recent studies also by the FETO consortium confirm that the data obtained with each parameter is not the same. Therefore, adding a combined use of all the different available predictors might improve the prediction of outcome.

These studies are part of ongoing efforts to develop reliable outcome prediction models, both at the time of diagnosis and after prenatal therapy. As suggested [4], we would like to caution the fetal medicine community prior to using this information. First, as shown by the same group, many of these measurements are not easily reproducible [5]. Second, as suggested by the same authors, it would be prudent to wait for external validation of these observations by other, independent researchers [2, 6]. Third, most of the data were collected on a small subset of patients with isolated left-sided CDH and severe pulmonary hypoplasia who underwent prenatal therapy. Clinical experience with FETO has, however, revealed significant individual variability in the response to FETO, both in lung size as well as vascularization [1–3, 7]. Fourth, at fetal surgery centers, the population of patients with less severe hypoplasia, and those who despite severe hypoplasia, are expectantly managed during pregnancy, are under-represented. It would be more comforting to know whether the pulmonary vascular assessment test can perform well also in the latter group of patients. In our opinion, until there is generalizable agreement upon the value, accuracy and validity of intrapulmonary Doppler, one should refrain from disclosing the prognostic information acquired by this particular investigational method to prospective research participants. The reason against disclosure is that, from an ethical viewpoint, patients have a right to all the information that is necessary to produce voluntary informed consent [8]. Informed consent should be provided only based on reliable, properly validated information. Because the present prediction model has not been validated in a wider research context, it does not provide (yet), when applied to individual patient-research subjects, reliable evidence of correct outcome prediction. In retrospect, patients might otherwise come to the conclusion that they have been wrongly included in a study, because of a wrong prediction of outcome based on an invalidated model. In addition, those with a poor Doppler prognosis after FETO might be misled in their decision either to continue that pregnancy or to terminate it, a legal right that most countries in Europe recognize to

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parents in these circumstances. Such situations put researchers at risk of liability and, more importantly, they may harm patients who having been given the correct facts, would either have not consented to participating in the study or would have withdrawn from it.

Centers managing fetuses with CDH, either expectantly or with FETO, would do well to test the proposed model in order to obtain proof of the validity and efficacy of pulmonary assessment in predicting survival and morbidity irrespective of prenatal intervention. The TOTAL trial (Tracheal Occlusion To Accelerate Lung growth) (www.totaltrial.eu) and the European-based observational study of FETO [9] present a great opportunity to do exactly that. Only when there is consensus and wide professional confidence in the results of the proposed combination of anatomical information (either observed/expected lung-to-head ratio or volume) should they be used to counsel patients towards their decision for considering FETO, another prenatal intervention, or expectant management during pregnancy. For the time being it seems logical to rely on lung size measurement, and perhaps position of the liver, as the best validated predictors, and informed consent should be provided based on their results [10, 11].

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